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"Flex-Activated" Mechanophores: Using Polymer Mechanochemistry To Direct Bond Bending Activation

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Supporting Information

ABSTRACT: We describe studies in mechanochemical transduction that probe the activation of bonds orthogonal to an elongated polymer main chain. Compression of mechanophore-cross-linked materials resulted in the release of small molecules via cleavage of covalent bonds that were not integral components of the elongated polymer segments. The reactivity is proposed to arise from the distribution of force through the cross-linking units of the polymer network and subsequent bond bending motions that are consistent with the geometric changes in the overall reaction. This departure from contemporary polymer mechanochemistry, in which activation is achieved primarily by force-induced bond elongation, is a first step toward mechanophores capable of releasing side-chain functionalities without inherently compromising the overall macromolecular architecture.

The study and control of mechanochemical transduction in macromolecular systems (i.e., polymer mechanochemistry) holds promise for addressing grand challenges in areas such as drug delivery, sensory materials, and autonomous self-healing systems and may also provide insights into how biological systems use physical impetuses to trigger chemical responses.[1] Precise control over the distribution of forces at the molecular level can be achieved through the development of polymeric materials capable of channeling elongational forces to mechanophores (i.e., functional groups that are designed to undergo selective bond scission in response to an external force). While ubiquitous in the natural world, synthetic analogues capable of this type of stimulus−response mechanism have only recently been developed. Within the past decade, investigations of the effects of mechanical stress upon polymeric materials have provided macromolecules capable of undergoing well-defined chemical changes in response to the application of mechanical force (Figure 1). By the introduction of a mechanophore at a specific point along the polymer chain, the application of stress to the polymer as a whole can be coupled to reactivity at a single site. Early efforts in mechanochemical control and design demonstrated the selective homolytic scission of weak covalent bonds[2] and site specificity.[3] Dative metal−ligand bonds have also been shown to be mechanochemically sensitive, giving rise to force-activated catalysts.[4] Additionally, ring-opening and cycloreversion reactions have provided exciting breakthroughs in force-guided reactivity, mechanochromics, and potential self-healing or -reinforcing materials. Key examples include opening of strained three- and four-membered rings,[5−8] formal retro-cycloaddition,[9−11] and electrocyclic ring opening of spiropyran chromophores.[12] Collectively, the assortment of demonstrated mechanochemical reactions accessible via polymer elongation spans a range of organic, organometallic, and inorganic transformations.

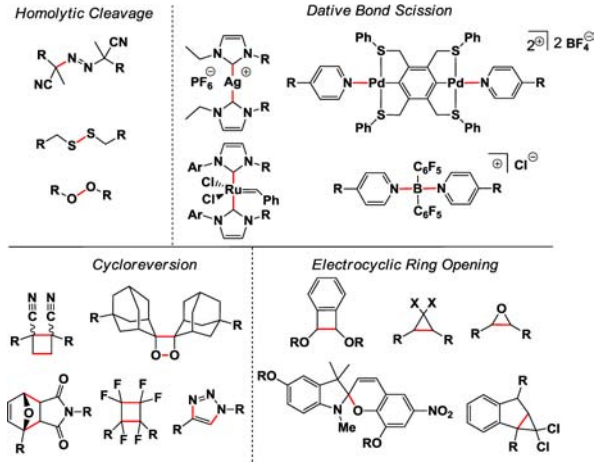

Figure 1. Generalized examples of moieties capable of mechanochemical activation, with the scissile bond(s) highlighted in red. R = site of polymer attachment; X = F, Cl.

A unifying theme in mechanophore designs aimed at bond scission remains an intuitive approach in which the bonds to be broken are integral components of the polymer main chains and thus are elongated in accordance with the general force vectors being applied to the flanking polymer segments. An exciting possibility would be the use of polymer scaffolds to control mechanochemical activation of bonds that are neither components of the main chain nor directly elongated by the tensile force within the polymer backbone.[13] This mode of reactivity could enable the release of small molecules from side chains while preserving the overall macromolecular structure and also provide new fundamental knowledge on how mechanical force can be coupled with chemical potential.

To investigate this idea, we considered the effects of bond angle distortions in modulating chemical reactivity. Geometric distortions can greatly influence the reactivity and ground-state hybridization, as observed in contemporary approaches toward Cu-free azide−alkyne cycloaddition and more traditional variations in, for example, carbonyl stretching frequencies in cyclic ketones with various ring sizes.[14] Mechanical activation of

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isolated small organic and inorganic molecules, metals and metalloids, and molecular dopants within polymer matrices has been intensely studied. In many instances, activation by shearing can occur through bond bending motions that augment ground-state geometries and lower HOMO−LUMO energy gaps.[1g,15,16] Recently, application of pressure to a polymer matrix doped with small-molecule mechanophores was found to catalyze mechanochemical isomerization. In this system, as opposed to ground-state destabilization, a negative activation volume for the reaction led to an overall lowering of the activation energy with increasing pressure.[17] In contrast, polymer mechanochemistry utilizes the macromolecular scaffold to direct force vectors to a covalently attached mechanophore in a precise manner. However, the use of this approach to accomplish activation primarily through transient bond angle distortions has not been fully investigated.

Application of stress causes a combination of conformational changes as a polymer chain is elongated, including both bond stretching and bending. In most cases, changes in bond angles require less energy than bond stretching and thus may provide an overall more efficient means of energy transduction. We envisioned that "flex activation" could occur in reactions in which the structural changes are consistent with the linearization that occurs during polymer elongation. An example of such reactivity would be cycloreversion reactions that convert main-chain alkene moieties into alkynes (Figure 2). Notably, although

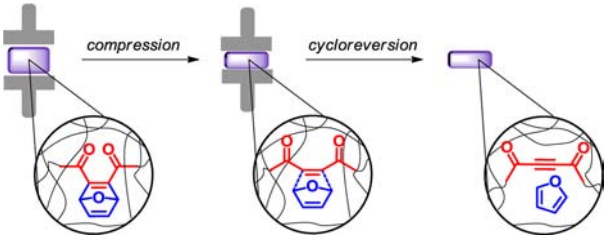


Figure 2. Generalized depiction of mechanophore activation via bond "flexing" motions induced by application of force.

the internuclear distance of the vinylic atoms would be lengthened in the overall transformation, the covalent bonds in the mechanophore that are located along the polymer main chain would actually become *shorter* and *stronger*. Herein we describe the results of our investigations into this new manifold for polymer mechanochemistry.

We considered oxanorbornadienes to be promising candidates to test our hypothesis that "flex activation" can be used in force-guided reactions. To model the effect of force upon the oxonorbornadiene architecture, we employed a modified version of the constrained geometries simulate external force (CoGEF) method developed by Beyer and recently demonstrated to be in good agreement with empirical reactivities of mechanophores.[6a,9c,18] Briefly, this method entails incremental distortions of the molecule along a specified coordinate, which upon relaxation of the rest of the molecule models the effects of mechanical force. As a simplified version of our experimental mechanophore, we applied this method to the oxanorbornadiene Diels−Alder adduct of furan and dimethyl acetylenedicarboxylate (DMAD). To mimic linearization of the ene−diester moiety, the angle θ indicated in Figure 3 was incrementally increased from its value in the ground-state geometry.[19] As can be seen in Figure 3, the expected increase in the calculated potential energy of the mechanophore was observed until the point at which cycloreversion occurred spontaneously. The value of ΔE just prior to

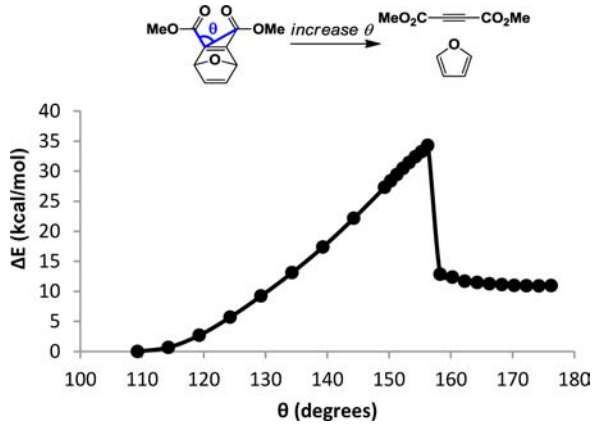
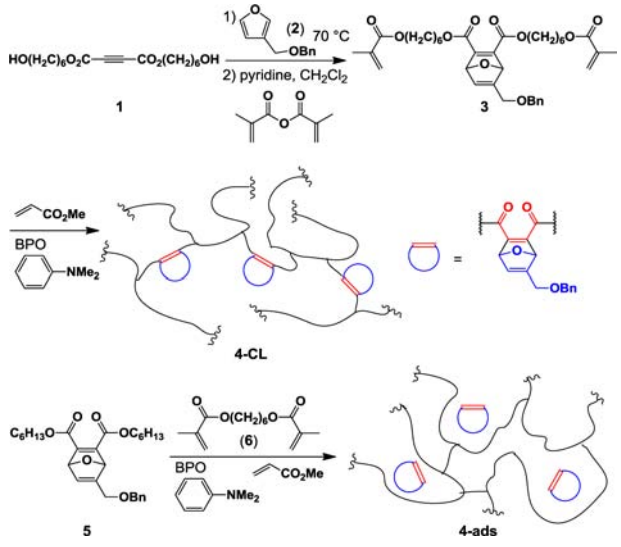


Figure 3. Calculated potential energies resulting from incremental increases in the angle θ. Density functional theory calculations were performed at the B3LYP 6-31G*(d) level using the Gaussian 09 program package.[20]

cycloreversion corresponded to an estimated activation energy (E_a) of 35 kcal/mol for the mechanochemical reaction. Importantly, this E_a value is well within the established range of mechanochemically accessible pathways.

Encouraged by the computational results, we prepared two types of cross-linked networks, each containing oxanorbornadiene mechanophores (Scheme 1): in one, the mechanophore

Scheme 1. Synthesis of the Network with Mechanophore Cross-Linking Units (4-CL) and the Control Network with Adsorbed Mechanophore Units (4-ads)



was used as a cross-linking unit that would experience extensional force upon application of stress; in the other, the mechanophore was adsorbed into a cross-linked material. Diol **1** was prepared from acetylenedicarboxylic acid and 1,6-hexanediol via Fischer esterification. Benzyl furfuryl ether (**2**) was chosen as the diene in place of furan to avoid issues of volatility with the latter. Diol **1** and furan **2** reacted smoothly via [4 + 2] cycloaddition to provide the corresponding oxanorbornadiene (not shown) in moderate yield. Subsequent reaction with methacryloyl anhydride furnished difunctionalized cross-linker mechanophore **3**. The cross-linked network **4-CL**, in which the mechanophore serves as the cross-linking unit, was prepared according to a procedure

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previously reported by Moore and co-workers.[7] For comparison, we also prepared mechanophore **5**, which is incapable of functioning as a cross-linking unit during acrylate polymerization. For this control system, 1,6-hexanediol dimethacrylate (**6**) was used as a cross-linker, ultimately providing a material in which the oxanorbornadiene mechanophore was adsorbed into the material but not covalently attached (**4-ads**). Copolymerization of a monoacrylate variant of **3** and methyl acrylate in the presence of benzoyl peroxide (BPO) and *N*,*N*-dimethylaniline confirmed the stability of the mechanophore under the polymerization conditions (see the Supporting Information).

After polymerization and cross-linking had ensued, each network was soaked in CH_2Cl_2 or MeOH for 2-h cycles to remove unincorporated small molecules. Multiple soak cycles were conducted until no additional small molecules were detected in the solution, as judged by GC−MS. The amounts of **3**, **5**, and **6** in the combined soak solutions were quantified and used to infer the amounts of these species that were incorporated into the cross-linked networks. By adjusting the feed ratios of the reactants, we prepared samples of **4-CL** with estimated mechanophore/cross-linker **3** contents of ca. 5 and 14 mol %. Similarly, samples of **4-ads** were prepared and determined to contain 17 mol % mechanophore **5** and 19 mol % cross-linker **6**; a **4-ads** network with lower mechanophore and cross-linker contents (7 and 11 mol %, respectively) was also prepared.

To evaluate the mechanochemical reactivity of each network, we conducted compression experiments on each sample at different pressures. Samples were loaded into a Carver press and subjected to sustained pressures as indicated in Figure 4. After 30

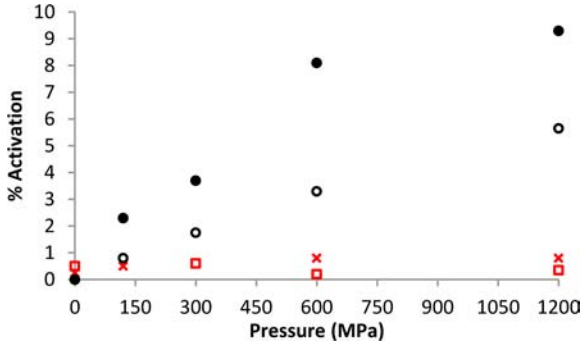

Figure 4. Plots of mechanophore % activation as a function of applied pressure, as judged by GC−MS analysis of soak solutions after compression of **4-CL** with 14 mol % **3** (black ●), **4-CL** with 5 mol % **3** (black ○), **4-ads** with 17 mol % **5** and 19 mol % **6** (red ×), and **4-ads** with 7 mol % **5** and 11 mol % **6** (red □). Each data point is an average of two independent compression experiments.

min of sustained stress, the sample was placed in CH_2Cl_2 to facilitate diffusion of released small molecules. The CH_2Cl_2 solutions were then analyzed by GC−MS and NMR spectroscopy. The GC−MS method was optimized to ensure that analysis of solutions containing **3** and **5** would not result in false-positive detection of **2**. Without applied stress, no furan was observed in the soak solution, indicating to us that no background amount of furan was released as a result of, for example, mechanochemical activation upon swelling or inadvertent physical adsorption during synthesis. Over the applied pressure range from 0 to 1200 MPa, we observed a monotonic increase in the % activation of the cross-linked mechanophore for both samples of **4-CL**. While the same trend was observed for **4-CL** containing 5 and 14 mol % mechanophore **3**, greater activation was observed from the network having a greater density of **3**. These results support a nonthermal activation mechanism, since thermal effects would be expected to influence the reactivity to the same extent in the two different variants of **4-CL**. Additionally, compression of **4-CL** for 1 min at 600 MPa gave essentially the same % activation (3.0%) as compression for 30 min (3.3%), consistent with mechanical activation mechanisms.[6c] Importantly, compression and analysis of each **4-ads** sample resulted in little or no activation at each pressure, further supporting the mechanochemical origins of the cycloreversion reaction. These results suggested to us that the released amounts of **2** detected in the compression experiments could not be attributed to thermal or pressure-induced activation.

Additional support for the proposed origin of **2** was obtained via confocal Raman spectroscopy (Figure 5). The spectra of

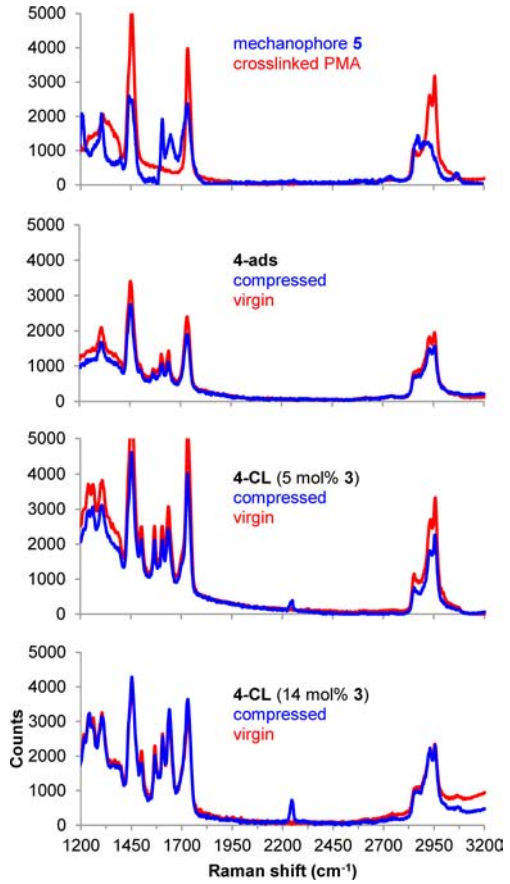

Figure 5. Raman spectra of (top to bottom) control mechanophore **5** and cross-linked PMA absent any mechanophore; network **4-ads** (17 mol % **5**) before and after compression at 1200 MPa for 30 min; **4-CL** (5 mol % **3**) before and after compression at 1200 MPa for 30 min; and **4-CL** (14 mol % **3**) before and after compression at 1200 MPa for 30 min. The spectra were recorded on highly ordered pyrolytic graphite with λ_{ex} = 785 nm.

control mechanophore **5** and poly(methyl acrylate) (PMA) cross-linked via incorporation of **6** without any mechanophore are shown in the top panel for reference. Prior to compression, the Raman spectrum of each **4-CL** sample showed only signals consistent with the mechanophore and the polymer network. After compression at 1200 MPa, each sample of **4-CL** displayed a new band at ca. 2250 cm^{-1}, consistent with known stretching frequencies of acetylenedicarboxylates. This indicated to us that

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cycloreversion with concomitant alkyne formation was the likely origin of **2**, consistent with the computational predictions and envisioned flex activation. The Raman spectra of **4-ads** before and after compression at 1200 MPa were essentially indistinguishable, and no alkyne formation was apparent.

In summary, we have demonstrated a fundamentally unique mechanochemical transduction process in mechanophores that undergo scission along bonds that are not components of the elongated polymer main chain, resulting in a net strengthening of the bonds in the polymer backbone. A unique aspect of the design is the use of the macromolecular scaffold to direct activation by means of bond bending induced by mechanical stress on the material. This "flex activation" method has been supported through experimental and computational studies. An exciting feature of these materials is their ability to undergo mechanochemical transduction to release small molecules capable of diffusing out of the polymer matrix. We anticipate that the successful development of flex-activated mechanophores will open a new avenue for the investigation of materials that respond to physical stimulus, both from the standpoint of mechanophore design and in the incorporation of these structures in advanced functional materials.

■ ASSOCIATED CONTENT

Supporting Information

Detailed experimental procedures, characterization of all new compounds, and complete ref 20. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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